

(a) an isolated nucleic acid molecule derived by *in vitro* mutagenesis from SEQ ID NO:3, SEQ ID NO:10, and SEQ ID NO:11; and

(b) an isolated nucleic acid molecule selected from the group consisting of human SVPH 4 DNA; an allelic variant of human SVPH 4 DNA; and a species homolog of SVPH 4 DNA.

### REMARKS

In the Written Opinion mailed 13 November 2000, the Authorized Officer asserts that claims 1-12 and 14 do not meet the requirements of Art. 33(2) because the Authorized Officer believes that the claimed subject matter is not new and embraces known subject matter, and points out that SEQ ID NO:1 is the known subject matter of EST X85598. In view of the amendments to claims 1-2, 5, and 13 to remove references to the nucleic acid molecule of SEQ ID NO:1 or the corresponding polypeptide of SEQ ID NO:4, Applicant believes that these claims now meet the requirement of Art. 33(2).

The Written Opinion further asserts that claim 1 does not meet the requirements of Art. 33(2) because claim 1(c), now presented as claim 1(d), did not define a minimal length of nucleic acids that hybridize under the specified conditions, and so such nucleic acids could encompass a trinucleotide. While Applicant disagrees with this assertion, because trinucleotides and other very short nucleic acids could never form stable nucleic acid hybrids under the hybridization and wash conditions specified by the claim, in view of the amendment to claim 1 to specify a minimum length for nucleic acids that hybridize, Applicant believes that claim 1 meets the requirement of Art. 33(2).

In addition, the Written Opinion states that the portions of claim 1 that were previously subparagraphs (d) and (f), relating to nucleic acids derived by mutagenesis, allelic variants, and species homologs, are considered to encompass any nucleic acid in the prior art. In view of the amendment to claim 1 to remove subparagraphs (d) and (f), Applicant believes that claim 1 meets the requirement of Art. 33(2).

In the Written Opinion, the Authorized Officer asserts that claim 13 does not meet the requirements of Art. 33(3) because the subject matter of claim 13 is considered to lack an inventive step, on the basis that any compound would solve the technical problem of

in membrane and cell-cell fusion, cellular adhesion, shedding of membrane proteins, and anti-coagulation, as described in the specification at page 3, lines 25-29. Far from being

presented with "an infinite number of equally possible solutions", the skilled person would recognize that there are a limited number of metalloproteinase-disintegrin polypeptides suitable to address the technical problem to which the specification is directed. Therefore, in view of the above and the amendment to claim 13 to clarify that the polypeptides of the claim are metalloproteinase-disintegrin polypeptides, Applicant believes that claim 13 meets the requirement of Art. 33(3).

The Written Opinion makes certain observations on the international application and the requirements of Article 6. The observations concerning what were previously claim 1 subparagraphs (c), (d), and (f) are considered by Applicant to be rendered moot by the amendments discussed above. With respect to the observation concerning use of the term "SVPH1 polypeptide" in claim 10, in light of the teaching of the specification and the reference in claim 10 to the host cell of claim 9 (and thus through claim 3 to the nucleic acids of claim 1), Applicant does not consider this term vague or unclear. However, in view of the amendment to claim 10 to refer instead to a polypeptide according to claim 4, Applicant believes any Article 6 concerns have been obviated.

Applicant has not been able to address the final observation of the Written Opinion, that "[c]laim 13 comprises all the features of claim 13 and is therefore not appropriately formulated as a claim dependent of the latter (Rule 6.4 PCT)", as it is unclear what was meant by this observation.

Please include the attached replacement sheets of claims with the pages originally filed in the international application.

Respectfully submitted,

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What is claimed is:

1. An isolated SVPH nucleic acid molecule selected from the group consisting of:
  - (a) an isolated nucleic acid molecule comprising a DNA sequence selected from the group consisting of SEQ ID NO:7, SEQ ID NO:8, and SEQ ID NO:9;
  - (b) an isolated nucleic acid molecule encoding an amino acid sequence comprising the sequence selected from the group consisting of SEQ ID NO:12, SEQ ID NO:13, and SEQ ID NO:14;
  - (c) an isolated nucleic acid molecule encoding an amino acid sequence comprising a sequence selected from the group consisting of amino acids 1 through 15 of SEQ ID NO:12, amino acids 16 through 188 of SEQ ID NO:12, amino acids 189 through 388 of SEQ ID NO:12, amino acids 389 through 491 of SEQ ID NO:12, amino acids 492 through 675 of SEQ ID NO:12, amino acids 676 through 698 of SEQ ID NO:12, amino acids 699 through 766 of SEQ ID NO:12, amino acids 699 through 787 of SEQ ID NO:13, and amino acids 699 through 820 of SEQ ID NO:14;
  - (d) an isolated nucleic acid molecule that comprises at least about 17 contiguous nucleotides and that hybridizes to either strand of a denatured, double-stranded DNA comprising a nucleic acid sequence of (c) under conditions of moderate stringency in 50% formamide and 6XSSC, at 42°C with washing conditions of 60°C, 0.5XSSC, 0.1% SDS; and
  - (e) an isolated nucleic acid molecule degenerate from SEQ ID NO:7, SEQ ID NO:8, and SEQ ID NO:9 as a result of the genetic code.
2. The nucleic acid molecule of claim 1 selected from the group consisting of SEQ ID NO:7, SEQ ID NO:8, and SEQ ID NO:9.
3. A recombinant vector that directs the expression of the nucleic acid molecule of claim 1.
4. An isolated polypeptide encoded by the nucleic acid molecule of claim 1.
5. An isolated polypeptide according to claim 4 having a molecular weight selected from the group consisting of approximately 86,983, 89,459, and 92,781 Daltons as determined by SDS-PAGE.
6. An isolated polypeptide according to claim 4 in non-glycosylated form.
7. Isolated antibodies that bind to a polypeptide of claim 4.
8. Isolated antibodies according to claim 7, wherein the antibodies are monoclonal.
9. A method for the production of a polypeptide according to claim 4 comprising culturing a host cell of claim 9 under conditions promoting expression.

11. The method of claim 10, wherein the host cell is selected from the group consisting of bacterial cells, yeast cells, plant cells, and animal cells.

12. The method of claim 10, wherein the host cell is a mammalian cell.

13. An isolated metalloproteinase-disintegrin polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, amino acids 1 through 15 of SEQ ID NO:12, amino acids 16 through 188 of SEQ ID NO:12, amino acids 189 through 388 of SEQ ID NO:12, amino acids 389 through 491 of SEQ ID NO:12, amino acids 492 through 675 of SEQ ID NO:12, amino acids 676 through 698 of SEQ ID NO:12, amino acids 699 through 766 of SEQ ID NO:12, amino acids 699 through 787 of SEQ ID NO:13, and amino acids 699 through 820 of SEQ ID NO:14.

14. An oligomer comprising a polypeptide of claim 4.

15. An isolated SVPH nucleic acid molecule selected from the group consisting of:

(a) an isolated nucleic acid molecule comprising a DNA sequence selected from the group consisting of SEQ ID NO:3, SEQ ID NO:10, and SEQ ID NO:11;

(b) an isolated nucleic acid molecule encoding an amino acid sequence comprising the sequence selected from the group consisting of SEQ ID NO:6, SEQ ID NO:15, SEQ ID NO:16, amino acids 686 through 713 of SEQ ID NO:15, amino acids 714 through 790 of SEQ ID NO:15, and amino acids 714 through 781 of SEQ ID NO:16;

(c) an isolated nucleic acid molecule encoding an amino acid sequence comprising a sequence selected from the group consisting of amino acids 1 through 27 of SEQ ID NO:15, amino acids 28 through 193 of SEQ ID NO:15, amino acids 194 through 392 of SEQ ID NO:15, amino acids 393 through 493 of SEQ ID NO:15, amino acids 494 through 685 of SEQ ID NO:15;

(d) an isolated nucleic acid molecule that comprises at least about 17 contiguous nucleotides and that hybridizes to either strand of a denatured, double-stranded DNA comprising a nucleic acid sequence of (c) under conditions of moderate stringency in 50% formamide and 6XSSC, at 42°C with washing conditions of 60°C, 0.5XSSC, 0.1% SDS; and

(e) an isolated nucleic acid molecule degenerate from SEQ ID NO:3, SEQ ID NO:10, and SEQ ID NO:11 as a result of the genetic code

16. The nucleic acid molecule of claim 15 selected from the group consisting of SEQ ID NO:3, SEQ ID NO:10, and SEQ ID NO:11.

17. A recombinant vector that directs the expression of the nucleic acid molecule of claim 15

18. An isolated polypeptide comprising an amino acid sequence selected from the group consisting of approximately 1/2, 1/3, 1/4, 1/5, and 1/6 of the amino acid sequence of the polypeptide of claim 4, determined by SDS-PAGE.

20. An isolated polypeptide according to claim 18 in non-glycosylated form.
21. Isolated antibodies that bind to a polypeptide of claim 18.
22. Isolated antibodies according to claim 21, wherein the antibodies are monoclonal antibodies.
23. A host cell comprising the vector of claim 17.
24. A method for the production of a polypeptide according to claim 18 comprising culturing a host cell of claim 23 under conditions promoting expression.
25. The method of claim 24, wherein the host cell is selected from the group consisting of bacterial cells, yeast cells, plant cells, and animal cells.
26. The method of claim 24, wherein the host cell is a mammalian cell.
27. An isolated metalloproteinase-disintegrin polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NO:6, SEQ ID NO:15, SEQ ID NO:16, amino acids 1 through 27 of SEQ ID NO:15, amino acids 28 through 193 of SEQ ID NO:15, amino acids 194 through 392 of SEQ ID NO:15, amino acids 393 through 493 of SEQ ID NO:15, amino acids 494 through 685 of SEQ ID NO:15, amino acids 686 through 713 of SEQ ID NO:15, amino acids 714 through 790 of SEQ ID NO:15, and amino acids 714 through 781 of SEQ ID NO:16.
28. An oligomer comprising a polypeptide of claim 18.
29. An isolated SVPH nucleic acid molecule selected from the group consisting of:
  - (a) the DNA sequence of SEQ ID NO:2;
  - (b) an isolated nucleic acid molecule encoding an amino acid sequence comprising the sequence of SEQ ID NO:5;
  - (c) an isolated nucleic acid molecule that hybridizes to either strand of a denatured, double-stranded DNA comprising the nucleic acid sequence of (a) or (b) under conditions of moderate stringency in 50% formamide and 6XSSC, at 42 °C with washing conditions of 60 °C, 0.5XSSC, 0.1% SDS;
  - (d) an isolated nucleic acid molecule derived by *in vitro* mutagenesis from SEQ ID NO:2;
  - (e) an isolated nucleic acid molecule degenerate from SEQ ID NO:2 as a result of the genetic code; and
  - (f) an isolated nucleic acid molecule selected from the group consisting of human
30. A recombinant vector that directs the expression of the nucleic acid molecule of

32. An isolated polypeptide encoded by the nucleic acid molecule of claim 29.
33. An isolated polypeptide according to claim 32 having a molecular weight of approximately 13,938 Daltons as determined by SDS-PAGE.
34. An isolated polypeptide according to claim 32 in non-glycosylated form.
35. Isolated antibodies that bind to a polypeptide of claim 32.
36. Isolated antibodies according to claim 35, wherein the antibodies are monoclonal antibodies.
37. A host cell transfected or transduced with the vector of claim 31.
38. A method for the production of SVPH 3 polypeptide comprising culturing a host cell of claim 37 under conditions promoting expression, and recovering the polypeptide from the culture medium.
39. The method of claim 38, wherein the host cell is selected from the group consisting of bacterial cells, yeast cells, plant cells, and animal cells.
40. The method of claim 38, wherein the host cell is a mammalian cell.
41. An isolated polypeptide comprising an amino acid sequence of SEQ ID NO:5.
42. An oligomer comprising a polypeptide of claim 32.
43. The nucleic acid molecule of claim 1 selected from the group consisting of
  - (a) an isolated nucleic acid molecule derived by *in vitro* mutagenesis from SEQ ID NO:7, SEQ ID NO:8, and SEQ ID NO:9; and
  - (b) an isolated nucleic acid molecule selected from the group consisting of human SVPH 1 DNA; an allelic variant of human SVPH 1 DNA; and a species homolog of SVPH 1 DNA.
44. The nucleic acid molecule of claim 12 selected from the group consisting of
  - (a) an isolated nucleic acid molecule derived by *in vitro* mutagenesis from SEQ ID NO:3, SEQ ID NO:10, and SEQ ID NO:11; and
  - (b) an isolated nucleic acid molecule selected from the group consisting of human SVPH 4 DNA; an allelic variant of human SVPH 4 DNA; and a species homolog of SVPH 4 DNA.